

**Guidance for Industry and FDA Reviewers**

**Content and Format of Premarket  
Notification [510(k)] Submissions for  
Liquid Chemical Sterilants/  
High Level Disinfectants**

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**This document supersedes Guidance on the Content and Format of Premarket Notification [510(k)]  
Submissions for Liquid Chemical Sterilants and High Level Disinfectants, December 18, 1997**



**U.S. Department Of Health And Human Services  
Food and Drug Administration  
Center for Devices and Radiological Health**

**Infection Control Devices Branch  
Division of Dental, Infection Control and General Hospital Devices  
Office of Device Evaluation**

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*Exhibit 1*

sterilants/high level disinfectants from regulation under FIFRA and the FDA classification process to exempt general purpose disinfectants from 510(k) requirements.

In 1996, the Food Quality Protection Act (FQPA) exempted liquid chemical sterilants/high level disinfectants used to process critical and semicritical medical devices from the definition of a pesticide under FIFRA and no longer regulates them. The FDA now has ~~sole~~ regulatory jurisdiction over liquid chemical sterilants/high level disinfectants used to process reusable critical and semicritical medical devices. The FQPA did not affect the regulatory authority over general purpose disinfectants; therefore, the MOU remains in effect for these products and the dual regulatory requirements continue until the FDA classifies and exempts them from 510(k) requirements.

In an effort to complete the classification rulemaking process, the FDA convened the General Hospital and Personal Use Devices Panel (Panel) in July 1995 to classify liquid chemical sterilants/high level disinfectants and general purpose disinfectants. The FDA Panel recommended that liquid chemical sterilants/high level disinfectants be classified as Class II devices (general and special controls) and that general purpose disinfectants be classified as Class I devices (general controls) and be exempted from 510(k) requirements. The FDA accepted the Panel's recommendation and published this classification plan as a proposed rule in the Federal Register on November 6, 1998 (Volume 63, Number 215, pages 59917-59921). When the FDA publishes the final classification rule, the rule will exempt the general purpose disinfectants from the FDA 510(k) requirements. The FDA currently regulates liquid chemical sterilants/high level disinfectants in the same manner as Class II devices; therefore, this final classification rule will only codify the current regulatory process.

This guidance document pertains only to liquid chemical sterilants/high level disinfectants used to process reusable critical and semicritical medical devices, and replaces the 1992 guidance document for liquid chemical germicides. The October 1993 draft document, "Guidance on the Content and Format of Premarket Notification [510(K)] Submissions for General Purpose Disinfectants" is available to provide specific guidance for a 510(k) submission of general purpose disinfectants until they are exempted.

#### **I.E. Device Modifications**

21 CFR 807.81 specifies that a premarket notification submission is required when significant modifications are made to a 510(k) cleared device. Persons intending to market a modified medical device should refer to the FDA document entitled, "Deciding When to Submit a 510(k) for a Change to an Existing Device ([www.fda.gov/cdrh/ode/510kmod.pdf](http://www.fda.gov/cdrh/ode/510kmod.pdf) or [www.fda.gov/cdrh/ode/510kmod.pdf](http://www.fda.gov/cdrh/ode/510kmod.pdf)).

The following modifications are examples of changes that may be made to 510(k) cleared liquid chemical sterilants/high level disinfectants but do not require a new 510(k) submission:

1. changes in containers/closures based on data from the FDA accepted stability protocols in the original 510(k)
2. additions to lists of compatible materials in labeling based on data from the FDA accepted test regimen described in the original 510(k)
3. changes to cleared directions for use that only clarify the directions
4. addition of new precautions, warnings, contraindications, or adverse effects
5. reduction in (or narrowing of) tolerances for ingredient specifications

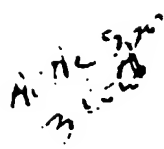

considered nonsignificant risk studies under 21 CFR Part 56, which do not require prior FDA approval under the Investigational Device Exemption (IDE).



### III.H.5. High Level Disinfection Claim

Support the high level disinfection claim with efficacy data from potency tests and with simulated- and in-use tests as outlined below.

#### a. Potency Tests

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- 1) FDA defines a high level disinfectant as a sterilant used under the same contact conditions except for a shorter contact time. Therefore, products with high level disinfection claims should first qualify as a sterilant by passing the Association of Official Analytical Chemists (AOAC) Sporicidal Test (Sporicidal Activity of Disinfectants, AOAC 6.3.05:1995, Official Method 966.04) as a sterilant, i.e., no failures in the full test with three separate product lots and under worst case conditions of germicide composition (as defined in Section III.H.3.a) when used according to labeling. Please note that the FDA will not accept partial AOAC Sporicidal Activity tests.
    - Submit a study report showing the results of complete testing. In the testing, include 60 carriers, representing each of two types of surfaces (porcelain penicylinders and silk suture loops). Test a total of 720 carriers or 240 carriers per product sample. Test the germicide against spores of both *Bacillus subtilis* ATCC 19659 and *Clostridium sporogenes* ATCC 3584 on three product samples representing three different batches. Use a contact time in the test that is comparable to the sterilization contact time for the claimed predicate germicide.
    - Obtain results of confirmatory tests conducted by an independent laboratory using one of the three lots used in the initial AOAC Sporicidal tests. When the FDA began actively regulating liquid chemical germicides in the early 1990's, we recommended efficacy testing that was consistent with the EPA efficacy data requirements for sterilizing or sporicidal agents (EPA DIS/TSS-9, July 11, 1985). Because precedence has been established, the FDA continues to recommend that the AOAC Sporicidal Test be conducted with a total of 720 carriers as described above.
    - Compare the AOAC Sporicidal Test contact times of the tested germicide and a legally marketed germicide consisting of a similar active ingredient. If there are significant differences between the contact times of the claimed predicate germicide and the new germicide, provide scientific justification, such as survivor curve analysis and the supporting data. Provide justification for the contact times by considering the practicality, material compatibility and microbicidal activity of the germicides.
    - Perform the AOAC Sporicidal Test as written in the most recent edition of the standard test recognized by the FDA. In a few special cases, a sponsor may consider deviations from the AOAC test, if they are scientifically justified. Consult the FDA prior to initiation of such testing.
  - 2) Once the product qualifies as a sterilant, conduct an additional potency test using the same contact conditions used for the AOAC Sporicidal Test except at a shorter contact
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time, as recommended in the labeling, in order to determine the time required to kill  $10^6$  organisms of an appropriate mycobacterium species, i.e., *Mycobacterium bovis* or *Mycobacterium terrae*. Use an alternative representative mycobacterium species if you can demonstrate with test data or literature references that the resistance of the organism to the chemical is similar to *Mycobacterium tuberculosis* var. *bovis*. The FDA recommends the modified (quantified) Tuberculocidal Activity of Disinfectants (AOAC 8.3.08:1995, Official Method 965.12) or a quantitative suspension test (Ascenzi et al., 1987).

- Conduct testing with the mycobacterium in suspension or on carriers, but quantify the number of organisms on the carriers.
- Run control carriers concurrently with the test group.
- Conduct testing with two of the three lots of product used for the AOAC Sporidical Test.

- 3) Submit study reports describing the microbiological lethality profile of the germicide under worst case conditions of germicide composition (See III.H.3.a). Use a contact time in each test shown below that is comparable to the contact time for the claimed predicate germicide. The proposed high level disinfectant should pass the following additional tests under the test conditions defined in the method noted:

- Fungicidal Activity of Disinfectants Using *Trichophyton mentagrophytes* (AOAC 8.3.02:1995, Official Method 955.17) - Conduct testing with one of the three lots of product used for the AOAC Sporidical Test.
- Testing Disinfectants Against *Salmonella choleraesuis*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*, Use-Dilution Methods (AOAC 8.2.01:1995, Official Methods 955.14, 955.15, and 964.02) - Conduct testing with one of the three lots of product used for the AOAC Sporidical Test.
- Virucidal Tests previously recommended by the EPA for its germicide registration program (DIS/TSS-7, November 12, 1981) - Conduct testing with one of the three lots of product used for the AOAC Sporidical Test.

For a list of the FDA recognized voluntary standard methods and supplemental information on these standard methods see <http://www.fda.gov/cdrh/modact/steril.html>. If testing was conducted according to these protocols, the firm may declare conformity to the recognized standard method and state any deviations from the standards that may apply (see Abbreviated 510(k) as described in Appendix D).

#### b. Simulated-use Testing

See Section III.H.4 for information about simulated-use testing. Use the most resistant mycobacterium species as the test organism. To support a high level disinfection claim, a test germicide should be able to kill at least  $10^6$  inoculated mycobacteria under the recommended contact time. For example, the FDA expects no survivors if the test device is challenged with a 6 log inoculum of mycobacterium. If failures occur, document and analyze each failure for causation, and then reevaluate the proposed label contact conditions for